IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	A.K. Gunnar Aberg, et al.
Serial No.	:	10/069,663
Filed	:	February 27, 2002
For	:	OPTICALLY ACTIVE ISOMERS OF KETOTIFEN AND THERAPEUTICALLY ACTIVE METABOLITES THEREOF
Examiner	:	Chang, Celia C.
Art Unit	:	1625
Attorney Docket No.	:	559P017
Confirmation No.	:	3512
Customer No.	:	42754

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents P.O. Box 1450, Alexandria, VA 22313-1450
on June 15, 2006 (Date)
Kevin S. Lemack
Name of applicant, assignee, or Registered Representative
Signature
June 15, 2006
Date

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

DECLARATION UNDER 37 C.F.R. §1.132

I, George E. Wright, hereby declare:

That I am a organic/medicinal chemist with over 38 years experience in academia and industry. After receiving the Ph.D. in pharmaceutical chemistry from the University of Illinois in 1967 and performing postdoctoral research at the University of Durham, England, I became Assistant Professor of Medicinal Chemistry at the University of Maryland in 1968. In 1974 I moved to the University of Massachusetts Medical School, Worcester, as Associate Professor of Pharmacology, and I was promoted to Professor of Pharmacology in 1978, a position that I held until

retirement from the University in 1998. I was founding Dean of Graduate Studies at the University of Massachusetts Medical School in 1979, and I spent sabbatical research years at the Institute of Experimental Physics, University of Warsaw, Poland (1980), and the Max Planck Institute for Medical Research, Heidelberg, Germany (1989). I have carried out basic organic and medicinal chemistry research and drug discovery research in the areas of antibiotics, antiviral and anticancer drugs, and I have guided numerous graduate students, postdoctoral fellows and staff scientists in related work.

I have worked in the areas of chiral drug molecule synthesis and analyses for more than 20 years and I have published over 150 research articles, reviews and book chapters in my areas of expertise. I am an inventor of 13 issued patents and 5 patents pending in various areas of organic medicinal chemistry and drug development;

That I have held the following positions:

1966-68	Senior Research Assistant, Department of Chemistry, University of Durham, England
1968-74	Assistant Professor of Medicinal Chemistry, University of Maryland School of Pharmacy, Baltimore, MD
1974-79	Associate Professor of Pharmacology, University of Massachusetts Medical School, Worcester, MA
1976-79	Affiliate Associate Professor, Department of Chemistry, Clark University, Worcester, MA
1978-80	Acting Associate Dean for Graduate Studies, University of Massachusetts Medical School, Worcester, MA.
1979-1998	Professor of Pharmacology, University of Massachusetts Medical School, Worcester, MA
1979-present	Affiliate Professor, Department of Chemistry, Clark University, Worcester, MA
1992-1995	Deputy Interim Chairman, Department of

	Pharmacology, University of Massachusetts Medical School, Worcester, MA
1980-84	Dean of Graduate Studies, University of Massachusetts Medical School, Worcester, MA
1980-81	Visiting Professor, Institute of Experimental Physics, University of Warsaw, Warsaw, Poland
1988-89	Fogarty Senior International Fellow, Department of Biophysics, Max Planck Institute for Medical Research, Heidelberg, Germany
1996-present	Founder and President, GLSynthesis Inc., Worcester, MA
1998-present	Professor of Pharmacology and Molecular Toxicology (Affiliate), University of Massachusetts Medical School, Worcester, MA

That I have reviewed the above-referenced patent application as well as the Office Actions, and I am familiar with its prosecution and the cited reference; and

That the term "substantially free of the corresponding R-isomer" has a well-known meaning in the art, is definite, and is commonly used in patent claim language.

1. The term "substantially free of the corresponding R-isomer" is a well-known term in the field of chiral chemistry. Chemists skilled in the art of chiral chemistry are well aware that absolute optical purity of a particular optical isomer is usually difficult, if not impossible, to achieve, particularly where the optical isomer is obtained from a racemic mixture as the starting material.

2. It is also known that occasionally, but very rarely, most or all of the biological activity of a racemic mixture can reside in one optical isomer thereof (the eutomer), and that unwanted side effects can reside in the other isomer (the distomer). In order to take advantage of this occurrence, those skilled in the

art appreciate that it is effective to provide pharmaceutical compositions that, in terms of optical purity, contain an amount of the distomer that is low enough to avoid the unwanted side effects. The term "substantially free of the corresponding R-isomer" is thus used to indicate that the composition can contain some amount of the distomer, but not so much that the undesired side effects are not avoided. Generally this amount is no more than about 10% of the distomer (90% of the eutomer). Those skilled in the art recognize that if the composition contains too much of the distomer, the advantageous effects of the eutomer are lost, and the composition is therefore not "substantially free" of the distomer.

3. Various issued U.S. patents illustrate the pervasive use of the term in question, and support my view of the above interpretation. See, for example, U.S. Patent No. 6,953,808. Column 5, lines 21-37 thereof define the term "substantially free of its (+)stereoisomer" to mean that "the compositions contain at least 90% by weight of (-)pantoprazole and 10% by weight or less of (+)pantoprazole." Note also claim 1, which recites administration of an amount of (-)pantoprazole, "substantially free of its (+)stereoisomer", sufficient to inhibit H^+, K^+-ATPase. See also U.S Patent No. 6,866,839, where the term "substantially free of the (S,S) stereoisomer" is defined at column 9, lines 17-20 to mean that the compositions contain at least about 90% of the eutomer and 10% or less of the distomer. See also Claim 72 of U.S. Patent No. 6,800,637 and column 3, lines 41-64.

4. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

George E. Wright, P.hD.

Date 6-2-06